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Prostate-specific antigen density as a prognostic marker in patients with localized prostate cancer

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BACKGROUND: The most important task in the field of improving the results of treatment of patients with prostate cancer (PCa) is their correct stratification by risk groups. Modern stratification systems do not fully provide an adequate risk assessment for all patients with prostate cancer. Further development of algorithms for predicting the clinical course of prostate cancer for a particular patient can positively affect the course and outcome of the disease.

AIM: Determination of the clinical and prognostic value of the density of prostate-specific antigen (PSAD) in patients with localized prostate cancer who underwent combined external beam radiation with androgen deprivation therapy.

MATERIALS AND METHODS: The effect of the PSAD parameter on the tumor-specific survival rates, as well as the clinical and morphological parameters of the tumor process, was assessed in 272 patients with localized prostate cancer who underwent combined external beam radiation with androgen deprivation therapy from January 1996 to July 2007.

RESULTS: The high clinical significance of the PSAD indicator has been demonstrated. An increase in PSAD correlated with an increase in serum PSA concentration, a decrease in PSA doubling time, and a decrease in tumor differentiation. The prognostic value of PSAD was confirmed in patients with localized prostate cancer who received combined hormone-radiation therapy. Using ROC-analysis, the threshold value of the PSAD index was determined – 0.36 ng / ml / cm^3, the excess of which was associated with a statistically significant decrease in the level of tumor-specific survival. The area under the curve was 0.703 (95% CI 0.236–0.434; $p < 0.001$). The risk of tumor-specific mortality and recurrence increased as the PSAD value increased.

CONCLUSION: The PSAD parameter is a reliable biomarker of prostate cancer with high rates of clinical and prognostic significance, the use of which is not associated with the introduction of costly and cumbersome methods of laboratory and instrumental diagnostics.

Keywords: prostate cancer; cancer-specific survival; prostate specific antigen; PCa; PCa density.

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Плотность простатспецифического антигена как прогностический маркер у больных локализованным раком предстательной железы

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Введение. Важнейшая задача в области улучшения результатов лечения больных раком предстательной железы — это их правильная стратификация по группам риска. Современные системы стратификации не позволяют в полной мере обеспечить адекватную оценку риска для всех больных раком предстательной железы. Дальнейшее развитие алгоритмов прогнозирования клинического течения рака предстательной железы для конкретного больного может положительным образом повлиять на течение и исход заболевания.

Цель. Определение клинического и прогностического значения плотности простатспецифического антигена (пПСА) у больных локализованным раком предстательной железы, перенесших комбинированное гормоно-лучевое лечение.

Материалы и методы. Проведена оценка влияния параметра пПСА на показатели опухоль-специфической выживаемости, а также клинико-морфологические параметры опухолевого процесса у 272 пациентов с локализованным раком предстательной железы, получавших комбинированное гормоно-лучевое лечение в период с января 1996 г. по июль 2007 г.

Результаты. Продемонстрирована высокая клиническая значимость показателя пПСА. Повышение пПСА коррелировало с увеличением концентрации сывороточного ПСА, снижением времени удвоения ПСА, уменьшением дифференцировки опухоли. Подтверждено прогностическое значение пПСА у пациентов с локализованным раком предстательной железы, получавших комбинированное гормоно-лучевое лечение. С помощью ROC-анализа определено пороговое значение показателя пПСА — 0,36 нг/(мл·см^3), превышение которого было связано со статистически значимым снижением уровня опухоль-специфической выживаемости. Площадь под кривой составила 0,703 (95 % ДИ 0,236–0,434; $p < 0,001$). Риск опухоль-специфической смертности и возникновения рецидива возрастает по мере увеличения показателя пПСА.

Заключение. Параметр пПСА является надежным биомаркером рака предстательной железы с высокими показателями клинической и прогностической значимости, использование которого не связано с внедрением затратных и обременительных методов лабораторной и инструментальной диагностики.

Ключевые слова: рак предстательной железы; опухоль-специфическая выживаемость; простатический специфический антиген; ПСА; плотность ПСА.

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ЭКО•ВЕКТОР

INTRODUCTION

Prostate cancer (PC) ranks second in prevalence among malignant neoplasms and ranks first among men aged >60 years in Russia [1]. Accurate prediction of the disease stage in patients with localized PC, despite the development of instrumental and laboratory diagnostic methods, still needs improvement. Prediction is based on digital rectal examination findings, initial concentration of serum prostate-specific antigen (PSA), and results of histological examination of prostate gland (PG) biopsies, namely, the degree of tumor differentiation according to the Gleason scale, percentage of the tumor in the biopsy sample, and presence of foci of perineural invasion [2–4]. The degree of tumor malignancy is a decisive factor in predicting and choosing the optimal treatment method; of all parameters, only the degree of tumor differentiation correlates significantly with the disease outcome [5]. Moreover, the PSA level and results of digital rectal examination without taking into account other clinical data are not significant prognostic factors, since they may be due to reasons not related to tumor lesion [6]. However, biopsy results do not allow a full assessment of PC characteristics such as the size, location, and morphology of the tumor lesion. The Gleason index is assigned based on the results of an assessment of a potentially heterogeneous tumor site and therefore does not accurately assess the entire volume and aggressiveness of the lesion focus in comparison with gross specimen examination after surgery [7]. The selection of treatment method is largely based on the assumption that the tumor characteristics according to the results of the primary biopsy reflect the true grade of malignancy. Thus, errors in assigning the total Gleason score can lead to overtreatment of patients with indolent tumors, and patients with aggressive tumors are undertreated, which will negatively affect disease outcomes. An accurate assessment of the tumor process characteristics will help distinguish patients who are suitable for active follow-up from those who need radical treatment and assess better the risk of further disease progression.

Despite the use of clinical and pathological parameters in practice, which in most cases provides acceptable risk stratification, prediction still needs improvement, which makes it difficult to choose the optimal treatment method in each case [8]. Thus, new prognostic biomarkers of PC should be identified [9].

PSA density (PSAd) is defined as the ratio of serum PSA to the PG volume. This indicator was originally used to assess the risk of PC among patients with baseline serum PSA concentration <10 ng/ml [10]. An increase in the concentration of serum PSA in benign prostatic hyperplasia (BPH) is associated with an increase in the volume of the glandular component of the PG, that is, the concentration of serum PSA increases in proportion to the increase in PG volume. In PC, the increase in PSA level is related to the invasive properties of the tumor, and its spread leads to an impairment of the acinar–vascular architectonics of the organ and PSA secretion directly into the systemic circulation. In patients with PC, PSAd is associated with both the tumor component and PG volume. Thus, the determination of PSAd allows for the assessment of the effect of BPH on the serum PSA concentration in patients with PC.

This study aimed to determine the clinical and prognostic values of PSAd in patients with localized PC who underwent combined hormone–radiation therapy.

MATERIALS AND METHODS

The retrospective study included 272 patients with localized PC (cT1-T2N0M0), who received combined hormone–radiation treatment at the Acad. A.M. Granov Russian Scientific Center for Radiology and Surgical Technologies in the period from January 1996 to July 2007 and were subsequently under case follow-up. The average age of the patients at the beginning of treatment was 66.5 ± 6.8 years. In patients included in the study, all data about the results of examination and treatment were available. Among these patients, the influence of the PSAd parameter on the indicators of tumor-specific survival, as well as the clinical and morphological parameters of the tumor process, was assessed.

In all patients, PSAd was calculated as the ratio of the baseline serum PSA concentration to the PG volume. The latter was assessed based on the results of ultrasound examination or magnetic resonance imaging of the PG. In the studied patients, PSAd ranged from 0.004 to 6.5 ng/(ml·cm^3), and the median PSAd was 0.45 ng/(ml·cm^3) (95% CI 0.41–0.52). The pathomorphological characteristics of the tumor according to the Gleason scale were assessed in 196 (72.1%) patients. Highly differentiated tumors (Gleason score ≤6) were detected in 98 (50.0%) patients, 67 (34.1%) patients had Gleason score of 7, and 31 (15.8%) patients had Gleason score of 8–10. The PSA doubling time in the study group ranged from 0.7 to 833.33 months, with a median value of 36.66 months (95% CI 26.84–40.00).

All patients with PC received combined hormone–radiation therapy. The average total focal dose to the target organ area (PG and seminal vesicles) was 67.01 ± 5.6 Gy. Hormone therapy was performed with gonadotropin-releasing hormone agonists and/or antiandrogenic drugs. To achieve the castrate level of testosterone, some patients underwent bilateral orchiectomy.

Statistical analysis of the data was performed using Statistica 10 En (StatSoft, Inc.), specifically with the *t*-test, Pearson χ^2-test, Fisher's exact test (*F*-test),

Mann–Whitney *U*-test, and receiver operating characteristic (ROC) analysis by plotting an ROC curve. Differences were considered significant at $p < 0.05$. The average values of the indicators are presented as with the standard deviation ($M \pm \sigma$).

RESULTS

At the first phase of the study, the tumor-specific survival rate of the studied patients was assessed. During the follow-up period, 48 patients died from the progression of the underlying disease (Table 1).

Table 1 shows the results of the univariate analysis and reveals that surviving and deceased patients were significantly different from each other with respect to the histological differentiation of the tumor tissues of the PG. Thus, highly differentiated tumors ($p < 0.0001$) were detected significantly more often in the surviving group, and poorly differentiated forms of PC are found in the deceased group ($p < 0.05$). The baseline serum PSA level was significantly lower in the surviving group than in the deceased group (15.06 and 22.45 ng/ml, respectively; $p = 0.0001$). Moreover, a significant difference was found in the PSA doubling time. This indicator was significantly higher in the surviving group (36.66 months) than in the deceased group (7.56 months) ($p < 0.01$). These groups have significantly different PSAd. The median PSAd in the surviving group was 0.42 ng/(ml·cm^3) and that in the deceased group was 0.66 ng/(ml·cm^3) ($p < 0.0001$).

The analysis of PSAd was performed if PC recurred after treatment. Tumor recurrence was noted in 52 patients. The median PSAd in patients with confirmed relapse was 0.74 ng/(ml·cm^3) (95% CI 0.63–0.93), and in those without relapse, it was 0.41 ng/(ml·cm^3) (95% CI 0.35–0.46) ($p < 0.001$).

In the second phase, the threshold value of PSAd was determined, and excess levels were associated with a significant decrease in tumor-specific survival rates. The ROC analysis was used to determine the threshold values of this parameter (Fig. 1, Table 2). The threshold value of PSAd was 0.36 ng/(ml·cm^3) with sensitivity and specificity levels of 89.58 and 46.43%, respectively.

In the third phase, we used the threshold value of PSAd to divide patients into groups of "low" and "high" PSAd (Table 3). In the "low" PSAd group, highly

Table 1. Main clinical and morphological parameters in surviving and deceased patients with prostate cancer ($n = 272$)

Таблица 1. Основные клинические и морфологические показатели у выживших и умерших пациентов с раком предстательной железы ($n = 272$)

Indicator	Surviving group ($n = 224$)	Deceased group ($n = 48$)	p
Age, years (*Me*, 95 % CI)	67.75, 67.14–68.67	66.87, 65.61–67.85	>0.05*
Follow-up period, months (*Me*, 95% CI)	147.0, 139.0–156.2	75.5, 63.7–100.0	<0.0001*
Baseline PSA level, ng/ml (*Me*, 95% CI)	15.06, 13.08–17.57	22.45, 18.81–28.21	0.0001*
PSAd, ng/(ml·cm^3) (*Me*, 95% CI)	0.42, 0.36–0.46	0.66, 0.57–0.90	<0.0001*
PSA doubling time, months (*Me*, 95% CI)	36.66, 30.46–40.00	7.56, 1.21–36.66	<0.01*
Gleason score:			
• <7	93 (41.5%)	5 (10.4%)	<0.0001**
• 7	54 (24.1%)	13 (27.0%)	>0.05**
• >7	20 (8.9%)	11 (22.9%)	<0.05***
• unknown	57 (25.4%)	19 (39.5%)	<0.05**
Total focal dose of local irradiation, Gy (*Me*, 95% CI)	68.0, 66.00–68.00	66.0, 66.00–68.00	>0.05*

Note. PSA, prostate-specific antigen; *Me*, median; 95% CI, 95% confidence interval. *Mann–Whitney *U*-test. ** χ^2 Pearson test. ****F*-test (Fisher's exact test).

Table 2. Characteristic of ROC-curve of values of the density of prostate-specific antigen in patients with localized prostate cancer

Таблица 2. Характеристика ROC-кривой значений плотности простатспецифического антигена у пациентов с локализованным раком предстательной железы

Area under the ROC curve	Root mean square error	p	Optimal criterion	95% CI	
				Lower limit	Higher limit
0.703	0.0363	<0.0001	0.3601	0.2360	0.4345

Table 3. Clinical and morphological parameters in patients with prostate cancer depending on values of the density of prostate-specific antigen (*n* = 272)

Таблица 3. Клинические и морфологические показатели у пациентов с раком предстательной железы в зависимости от значений плотности простатспецифического антигена (*n* = 272)

Aspect analyzed	Low PSAd (*n* = 101)	High PSAd (*n* = 171)	*p*
Age, years (*Me*, 95% CI)	68.33, 67.21–69.56	66.92, 64.92–67.65	>0.05*
Baseline PSA level, ng/ml (*Me*, 95% CI)	9.8, 8.00–11.30	23.00, 20.35–26.07	<0.0001*
PSA doubling time, months (*Me*, 95% CI)	40.00, 36.66–47.73	24.60, 13.97–36.66	<0.001*
Gleason score:			
• <7	63 (62.3%)	35 (20.4%)	<0.0001**
• 7	14 (13.8%)	53 (30.9%)	<0.01**
• >7	9 (8.3%)	22 (12.8%)	>0.05***
• unknown	15 (14.8%)	61 (35.6%)	<0.001**

Note. PSA, prostate-specific antigen; *Me*, median; 95% CI, 95% confidence interval. *Mann–Whitney *U*-test. ** χ^2 Pearson test. ****F*-test (Fisher's exact test).

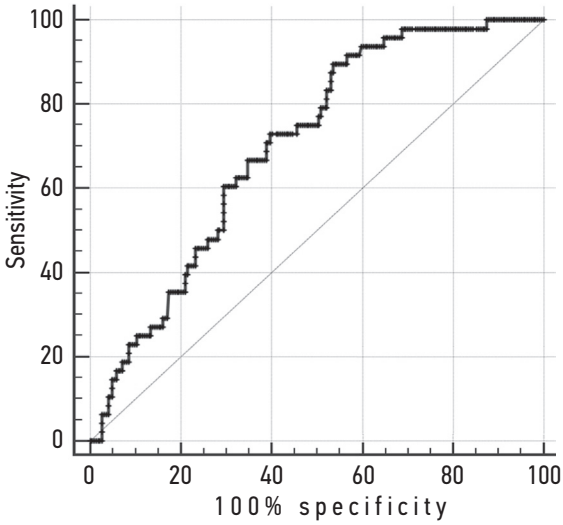

Fig. 1. Results of ROC-analysis of values of the density of prostate-specific antigen in patients with localized prostate cancer

Рис. 1. Результаты ROC-анализа значений плотности простатспецифического антигена у пациентов с локализованным раком предстательной железы

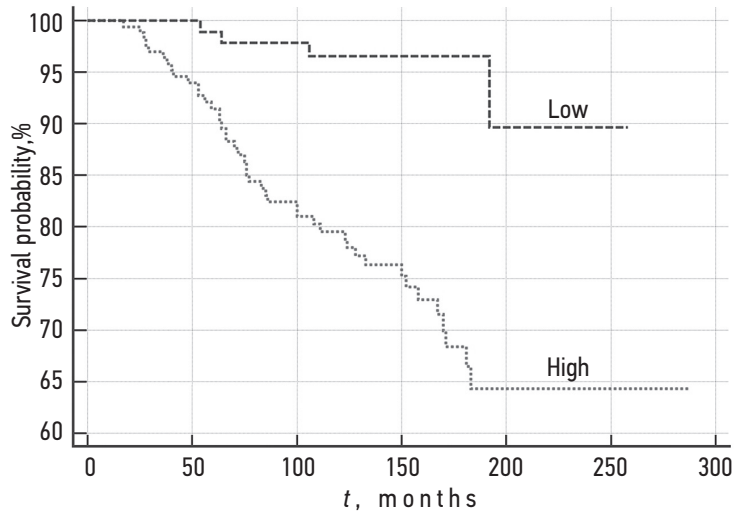

Fig. 2. Cancer-specific survival prostate cancer patients with "high" and "low" density of prostate-specific antigen

Рис. 2. Опухоль-специфическая выживаемость пациентов с локализованным РПЖ с «высокой» и «низкой» плотностью простатспецифического антигена

differentiated PC was detected significantly more often, and "moderately differentiated" tumors were revealed significantly more often in the "high" PSAd group. The baseline serum PSA concentration was significantly lower in the "low" PSAd group. The PSA doubling time increased with decreasing PSAd. Figure 2 shows the results of the assessment of the tumor-specific survival of patients with PC, depending on PSAd.

As the cumulative proportion of survivors did not decrease below 50% during the follow-up period, the median tumor-specific survival was not achieved. The average tumor-specific survival in the "low" PSAd group was 247.21 (95% CI 236.27–258.15) months, and it was 222.64 (95% CI 206.29–238.98) months in the "high" PSAd group. In the "low" and "high" PSAd groups, the 1-year tumor-specific survival rate of patients with localized PC reached 100%, the 5-year survival rates were 98.9% ± 1.0% and 91.5% ± 2.1%, and the 10-year survival rates were 96.6% ± 1.9% and 79.6% ± 3.2%, respectively. The relative risk of death in the "high" PSAd group increased 3.6 times compared with that in the "low" PSAd group (95% CI 2.0139–6.4446). Thus, in patients with localized PC, lower PSAd was accompanied by better tumor-specific survival rates.

DISCUSSION

Malignant PG tumor tissues are known to release into the systemic circulation (per unit volume) about 10 times more PSA than did benign PG tissues [11]. Unlike most developed countries, with the introduction of serum PSA-based screening, the number of newly diagnosed PC cases has increased and the number of deaths has decreased [12]; in Russia, we registered a steady increase

in mortality rates from this disease [10]. In 1992, Benson et al. [13] proposed the concept of PSAd to neutralize the effect of the PG volume on the serum PSA level. Subsequently, several studies have demonstrated that PSAd > 0.15 ng/(ml·cm^3) is associated with a significantly higher probability of PC detection [14–16].

To our knowledge, this study is one of the few studies that focused on the analysis of the relationship between PSAd and outcomes of hormone–radiation treatment in patients with localized PC [17–19]. We have demonstrated the high clinical and prognostic significance of this parameter in this group. Thus, in patients with higher PSAd, the degree of histological differentiation of the tumor was lower, the initial serum PSA level was higher, and the PSA doubling time was shorter, which indicates a higher tumor growth rate. Furthermore, patients with localized PC with high PSAd have a higher risk of tumor-specific mortality and recurrence after treatment.

CONCLUSION

The results obtained suggest that PSAd is a reliable biomarker of PC with high rates of clinical and prognostic significance, and its use is not associated with the introduction of expensive and cumbersome laboratory methods and instrumental diagnostics.

ADDITIONAL INFORMATION

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Conflict of interest. The authors declare no conflict of interest.

REFERENCES

1. *Zlokachestvennye novoobrazovanija v Rossii v 2018 godu* (zabolevaemost' i smertnost'). Kaprina AD. Starinskogo VV, Petrovoj GV., editors. Moscow: MNIOI. PA. Gercena filial FGBU "NMIC radiologii" Minzdrava Rossii. 2019. 250 p.

2. Partin AW, Kattan MW, Subong EN, et al. Combination of prostate-specific antigen, clinical stage, and Gleason score to predict pathological stage of localized prostate cancer. A multi-institutional update. *JAMA*. 1997;277(18):1445–1451.

3. D'Amico AV, Whittington R, Malkowicz SB, et al. Combined modality staging of prostate carcinoma and its utility in predicting pathologic stage and postoperative prostate specific antigen failure. *Urology*. 1997;49(3A Suppl):23–30. DOI: 10.1016/S0090-4295(97)00165-9

4. Ramos N, Macedo A, Rosa J, Carvalho M. Perineural invasion in prostate needle biopsy: Prognostic value on radical prostatectomy and active surveillance. *Arch Ital Urol Androl*. 2020;92(4). DOI: 10.4081/aiua.2020.4.330

5. Brimo F, Montironi R, Egevad L, et al. Contemporary grading for prostate cancer: implications for patient care. *Eur Urol*. 2013;63(5):892–901. DOI: 10.1016/j.eururo.2012.10.015

6. Wilkinson BA, Hamdy FC. State-of-the-art staging in prostate cancer. *BJU Int*. 2001;87(5):423–430. DOI: 10.1046/j.1464-410x.2001.02146.x

7. Sved PD, Gomez P, Manoharan M, et al. Limitations of biopsy Gleason grade: implications for counseling patients with biopsy Gleason score 6 prostate cancer. *J Urol*. 2004;172(1):98–102. DOI: 10.1097/01.ju.0000132135.18093.d6

8. Saad F, Latour M, Lattouf JB, et al. Biopsy Based Proteomic Assay Predicts Risk of Biochemical Recurrence after Radical Prostatectomy. *J Urol*. 2017;197(4):1034–1040. DOI: 10.1016/j.juro.2016.09.116

9. Zhang Y, Zhang P, Wan X, et al. Downregulation of long non-coding RNA HCG11 predicts a poor prognosis in prostate cancer. *Biomed Pharmacother*. 2016;83:936–941. DOI: 10.1016/j.biopha.2016.08.013

10. Benson MC, Whang IS, Pantuck A, et al. Prostate specific antigen density: a means of distinguishing benign prostatic hypertrophy and prostate cancer. *J Urol*. 1992;147(3 Pt 2):815–816. DOI: 10.1016/s0022-5347(17)37393-7

11. Kanehara H, Ueda H, Katsuoka Y. [The efficacy of PSA density for the early detection of prostate cancer]. *Nihon Rinsho*. 1998;56(8):2012–2015. (In Japan.)

12. Tarone RE, Chu KC, Brawley OW. Implications of stage-specific survival rates in assessing recent declines in prostate cancer mortality rates. *Epidemiology*. 2000;11(2):167–170. DOI: 10.1097/00001648-200003000-00014

13. Benson MC, Whang IS, Olsson CA, et al. The use of prostate specific antigen density to enhance the predictive value of intermediate levels of serum prostate specific antigen. *J Urol*. 1992;147(3 Pt 2):817–821. DOI: 10.1016/s0022-5347(17)37394-9

14. Presti JC Jr, Hovey R, Carroll PR, Shinohara K. Prospective evaluation of prostate specific antigen and prostate specific antigen density in the detection of nonpalpable and stage T1C carcinoma of the prostate. *J Urol*. 1996;156(5):1685–1690.

15. Ohori M, Wheeler TM, Dunn JK, et al. The pathological features and prognosis of prostate cancer detectable with current diagnostic tests. *J Urol*. 1994;152(5 Pt 2):1714–1720. DOI: 10.1016/s0022-5347(17)32369-8

16. Epstein JI, Sanderson H, Carter HB, Scharfstein DO. Utility of saturation biopsy to predict insignificant cancer at radical prostatectomy. *Urology*. 2005;66(2):356–360. DOI: 10.1016/j.urology.2005.03.002

17. Zentner PG, Pao LK, Benson MC, et al. Prostate-specific antigen density: a new prognostic indicator for prostate cancer. *Int J Radiat Oncol Biol Phys*. 1993;27(1):47–58. DOI: 10.1016/0360-3016(93)90420-z

18. Corn BW, Hanks GE, Lee WR, et al. Prostate specific antigen density is not an independent predictor of response for prostate cancer treated by conformal radiotherapy. *J Urol*. 1995;153(6):1855–1859

19. Pollack A, Lankford S, Zagars GK, Babaian RJ. Prostate specific antigen density as a prognostic factor for patients with prostate carcinoma treated with radiotherapy. *Cancer*. 1996;77(8):1515–1523. DOI: 10.1002/(SICI)1097-0142(19960415)77:8<1515

СПИСОК ЛИТЕРАТУРЫ

1. Злокачественные новообразования в России в 2018 году (заболеваемость и смертность). Под ред. А.Д. Каприна, В.В. Старинского, Г.В. Петровой. М.: МНИОИ им. П.А. Герцена — филиал ФГБУ «НМИЦ радиологии» Минздрава России. 2019. 250 с. Режим доступа: https://oncology-association.ru/wp-content/uploads/2020/09/2018.pdf Дата обращения: 09.08.2021.

2. Partin A.W., Kattan M.W., Subong E.N., et al. Combination of prostate-specific antigen, clinical stage, and Gleason score to predict pathological stage of localized prostate cancer. A multi-institutional update // JAMA. 1997. Vol. 277, No. 18. P. 1445–1451.

3. D'Amico A.V., Whittington R., Malkowicz S.B., et al. Combined modality staging of prostate carcinoma and its utility in predicting pathologic stage and postoperative prostate specific antigen failure // Urology 1997. Vol. 49, No. 3A Suppl. P. 23–30. DOI: 10.1016/S0090-4295(97)00165-9

4. Ramos N., Macedo A., Rosa J., Carvalho M. Perineural invasion in prostate needle biopsy: Prognostic value on radical prostatectomy and active surveillance // Arch Ital Urol Androl. 2020. Vol. 92. No. 4. DOI: 10.4081/aiua.2020.4.330

5. Brimo F., Montironi R., Egevad L., et al. Contemporary grading for prostate cancer: implications for patient care // Eur Urol. 2013. Vol. 63, No. 5. P. 892–901. DOI: 10.1016/j.eururo.2012.10.015

6. Wilkinson B.A., Hamdy F.C. State-of-the-art staging in prostate cancer // BJU Int. 2001. Vol. 87, No. 5. P. 423–430. DOI: 10.1046/j.1464-410x.2001.02146.x

7. Sved P.D., Gomez P., Manoharan M., et al. Limitations of biopsy Gleason grade: implications for counseling patients with biopsy Gleason score 6 prostate cancer // J Urol. 2004. Vol. 172, No. 1. P. 98–102. DOI: 10.1097/01.ju.0000132135.18093.d6

8. Saad F., Latour M., Lattouf J.B., et al. Biopsy Based Proteomic Assay Predicts Risk of Biochemical Recurrence after Radical Prostatectomy // J Urol. 2017. Vol. 197, No. 4. P. 1034–1040. DOI: 10.1016/j.juro.2016.09.116

9. Zhang Y., Zhang P., Wan X., et al. Downregulation of long non-coding RNA HCG11 predicts a poor prognosis in prostate cancer // Biomed Pharmacother. 2016. Vol. 83. P. 936–941. DOI: 10.1016/j.biopha.2016.08.013

10. Benson M.C., Whang I.S., Pantuck A., et al. Prostate specific antigen density: a means of distinguishing benign prostatic hypertrophy and prostate cancer // J Urol. 1992. Vol. 147, No. 3 Pt 2. P. 815–816. DOI: 10.1016/s0022-5347(17)37393-7

11. Kanehara H., Ueda H., Katsuoka Y. [The efficacy of PSA density for the early detection of prostate cancer] // Nihon Rinsho. 1998. Vol. 56, No. 8. P. 2012–2015. (In Japan.)

12. Tarone R.E., Chu K.C., Brawley O.W. Implications of stage-specific survival rates in assessing recent declines in prostate cancer mortality rates // Epidemiology. 2000. Vol. 11, No. 2. P. 167–170. DOI: 10.1097/00001648-200003000-00014

13. Benson M.C., Whang I.S., Olsson C.A., et al. The use of prostate specific antigen density to enhance the predictive value of intermediate levels of serum prostate specific antigen // J Urol. 1992. Vol. 147, No. 3, Pt 2. P. 817–821. DOI: 10.1016/s0022-5347(17)37394-9

14. Presti J.C., Jr., Hovey R., Carroll P.R., Shinohara K. Prospective evaluation of prostate specific antigen and prostate specific antigen density in the detection of nonpalpable and stage T1C carcinoma of the prostate // J Urol. 1996. Vol. 156, No. 5. P. 1685–1690.

15. Ohori M., Wheeler T.M., Dunn J.K., et al. The pathological features and prognosis of prostate cancer detectable with current diagnostic tests // J Urol. 1994. Vol. 152, No. 5, Pt 2. P. 1714–1720. DOI: 10.1016/s0022-5347(17)32369-8

16. Epstein J.I., Sanderson H., Carter H.B., Scharfstein D.O. Utility of saturation biopsy to predict insignificant cancer at radical prostatectomy // Urology. 2005. Vol. 66, No. 2. P. 356–360. DOI: 10.1016/j.urology.2005.03.002

17. Zentner P.G., Pao L.K., Benson M.C., et al. Prostate-specific antigen density: a new prognostic indicator for prostate cancer // Int J Radiat Oncol Biol Phys. 1993. Vol. 27, No. 1. P. 47–58. DOI: 10.1016/0360-3016(93)90420-z

18. Corn B.W., Hanks G.E., Lee W.R., et al. Prostate specific antigen density is not an independent predictor of response for prostate cancer treated by conformal radiotherapy // J Urol. 1995. Vol. 153, No. 6. P. 1855–1859

19. Pollack A., Lankford S., Zagars G.K., Babaian R.J. Prostate specific antigen density as a prognostic factor for patients with prostate carcinoma treated with radiotherapy // Cancer. 1996. Vol. 77, No. 8. P. 1515–1523. DOI: 10.1002/(SICI)1097-0142(19960415)77:8<1515

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